REMARKS/ARGUMENTS

35 USC §112 – Claims 26, 32 and 34

The Examiner has maintained the rejection to claims 26, 32 and 34 for lack of enablement. Claims 26, 32, and 34 have been amended to remove the term "pharmaceutical", as it appears in the expressions "[a] pharmaceutical composition comprising ..." and "active pharmaceutical ingredient". Accordingly, withdrawal of the rejection to these claims is respectfully requested.

35 USC §102(b) - Claims 5 and 39

The Examiner has reapplied Yoneyama *et al.* alleging that claims 5 and 39 lack novelty. The Examiner argues that the isolated phosphorylated IRF-3 protein disclosed by Yoneyama *et al.* following NDV infection causes an increase in interferon expression and that virus infection inherently results in phosphorylation of IRF-3 in the serine or threonine phosphoacceptor site in the carboxy terminus.

Applicant respectfully disagrees that Yonehama *et al.* inherently anticipates the claimed subject matter. U.S. case law has held that an inherency question is not based on whether a prior art process inherently results in a claimed invention, but whether one of skill in the art would read a prior art reference as inherently disclosing an invention.

Yonehama et al.

The experimental results of the Yonehama *et al.* reference reveal that substitution of Ser-385 and Ser-386 with alanine creates an inactive form of the IRF3 protein which does not stimulate cytokine gene activation. This behavior was described as comparable to deletion of carboxy-terminal residues 375-427 that results in no inducible phosphorylation or transactivation. In other words, Yoneyama *et al.* do not disclose mutation of serine (or threonine) residues in the carboxy terminus with a serine-threonine phosphomimetic such that the protein behaves as if it was phosphorylated. Therefore, while Yonehama *et al.* may have demonstrated IRF-3 inactivation, they did not show IRF-3 activation through phosphorylation. Accordingly, a person of skill in the art would not have recognized that a modified serine or threonine phosphoacceptor site would have caused cytokine gene activation by the IRF protein that is increased relative to cytokine gene activation by a corresponding wild type IRF protein as claimed.

Inherent Anticipation

The U.S. courts have summarized a two-prong test for inherent anticipation in determining whether the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. The first test to finding inherent anticipation is that the undisclosed element of the prior art has to be a necessary technological fact of the prior art (here, virus infection resulting in phosphorylation of IRF-3 in the serine or threonine phosphoacceptor site in the carboxy terminus). It is inadequate to show

that the prior art process would probably, or possibly, produce the undisclosed element. Rather, the undisclosed element has to flow as a natural consequence from the technological constraints of the prior art. In other words, absent a showing that virus infection results in phosphorylation of IRF-3 in the serine or threonine phosphoacceptor site in the carboxy terminus, a finding of inherent anticipation would be improper. Since Yonehama *et al.* demonstrated IRF-3 inactivation, clearly IRF-3 activation through phosphorylation does not flow as a natural consequence from the reference.

The second test to finding inherent anticipation is that a person of ordinary skill in the art be able to recognize the undisclosed element is a natural characteristic of the prior art. Inherency cannot be based on the inventor's own disclosure, and facts asserted to be inherent in the prior art must be shown by evidence from the prior art. Broader speculation of the characteristics of the prior art is deemed inappropriate for an anticipation analysis and should instead be reserved for an obviousness inquiry (here, virus infection resulting in phosphorylation of IRF-3 in the serine or threonine phosphoacceptor site in the carboxy terminus). It appears that extracts isolated from the reference (i.e. NDV infection causes an increase in interferon expression), aided by hindsight in view of the teachings of the instant application (i.e. phosphorylation of IRF-3 in the serine or threonine phosphoacceptor site in the carboxy terminus) have led the Examiner to incorrectly conclude that the invention is inherently anticipated by Yonehama *et al.*.

The U.S. courts recently addressed anticipation by inherency in *Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education* (346 F.3d 1051, 1054 (Fed. Cir. 2003)). The defendant challenged the validity of the Elan claims as inherently anticipated by a reference by Mullan. The claims in question were directed to transgenic mice that were transformed with a gene that produced a human mutated protein. The defendant alleged that use of the standard procedures set forth in Mullan would enable a skilled person to produce a statistically small percentage of transgenic mice capable of producing a human mutated protein. Although Mullan described known procedures for making a transgenic animal, he neither described every element of the claims, nor taught, in terms other than by trial and error and hope, production of a transgenic mouse having the human protein. While Mullan may have had the concept of creating a transgenic mouse, Mullan did not make such a mouse and he did not tell (or know) which, if any, of the standard procedures from the scientific literature might be effective in achieving the complex series of transformations needed for a successful product. Thus, neither Mullan nor anyone else (1) had made a mouse harboring the mutated gene, (2) knew whether the mouse DNA would accept the mutated gene, or (3) knew if the mouse cell would then express the human mutated protein.

The court held that a general recitation of known procedures, none of which was carried out by Mullan, does not defeat the "novelty" of the specific mouse that was actually produced by Elan. In other words, general instructions to conduct failure-prone activities such as gene transfer between humans and animals, and the ensuing uncertainties with respect to gene expression do not meet the legal criteria of anticipation. Extrapolating this line of analysis to the instant case, it could similarly be argued that while Yoneyama *et al.* demonstrated substitution of the serine residues at 385 and 386 to alanine created an inactive form of the IRF3 protein, they did not produce active versions of the same protein. In addition, they did not know, which, if any, of the

remaining serine residues might be phosphorylated to generate an active form of the IRF3 protein. Thus, a skilled person would not have recognized or appreciated the inherent feature (i.e. phorphorylation of the Ser and Thr residues in the carboxy terminus) in the Yoneyama *et al.* reference.

In summary, inherent properties of prior art should be limited to the technological facts of the references. Once it is determined that an undisclosed property is an inherent technological fact of a reference, then it is proper to ask whether reasonably skilled artisans would recognize the property as a fact. For example, physical properties such as melting points and solubility characteristics are such inherent properties or characteristics (see *In re Donohue*, 766 F.2d 531, 534, 226 U.S.P.Q. (BNA)) . However, certain characteristics such as phosphorylation of IRF-3 serine or threonine residues, although possibly or probably a property of a reference, are not inherent to that reference and are insufficient to support inherent anticipation. Until it is determined that an unexpressed characteristic of a reference is a necessary technological fact, the common knowledge of artisans should not be introduced into an anticipation analysis.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection.

35 USC §102(a) - Claims 5 to 7 and 39

The Examiner has rejected claims 5 to 7 and 39 as anticipated by Lin *et al.* under 35 USC §102(a).

35 USC § 102(a) states that a person shall be entitled to a patent unless:

> *the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent* ... [Emphasis added.]

The wording of 35 USC §102(a) distinguishes an invention between "the applicant" and "others". Accordingly, knowledge in any form possessed only by the applicant, or use made only by the applicant, and/or inventor-derived printed publications may not serve as prior art against such applicant under 35 USC §102(a). In this respect, an affidavit under 37 CFR §1.132 is submitted herewith by the inventors attesting that the Lin *et al.* reference is their earlier work and therefore, is not a reference invention by "another". Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

In view of the forgoing, early favorable consideration of this application is earnestly solicited.

It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, he is invited to contact Elizabeth Hayes-Quebec at (613) 232-2486.

Respectfully submitted,

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